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1: J Mol Biol 1998 Dec 11;284(4):1141-51

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The fibronectin type III domain as a scaffold for novel binding proteins.

Koide A, Bailey CW, Huang X, Koide S.

Department of Biochemistry and Biophysics, University of Rochester Medical Center, Rochester, NY, 14642, USA.

The fibronectin type III domain (FN3) is a small autonomous folding unit which occurs in many animal proteins involving in ligand binding. The beta-sandwich structure of FN3 closely resembles that of immunoglobulin domains. We have prepared a phage display library of FN3 in which residues in two surface loops were randomized. We have selected mutant FN3s which bind to a test ligand, ubiquitin, with significant affinities, while the wild-type FN3 shows no measurable affinity. A dominant clone was expressed as a soluble protein and its properties were investigated in detail. Heteronuclear NMR characterization revealed that the selected mutant protein retains the global fold of FN3. It also has a modest conformational stability despite mutations at 12 out of 94 residues. These results clearly show the potential of FN3 as a scaffold for engineering novel binding proteins. Copyright 1998 Academic Press.

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